

Fig. 1

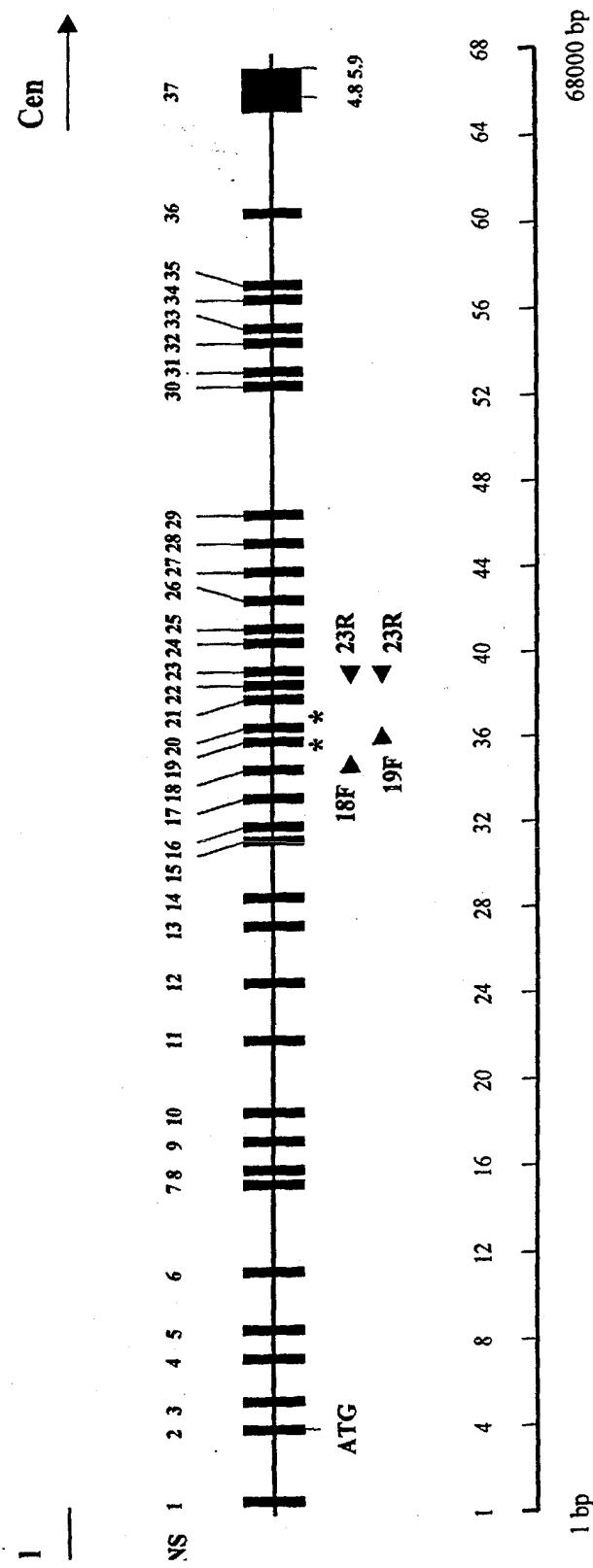


Fig. 2a

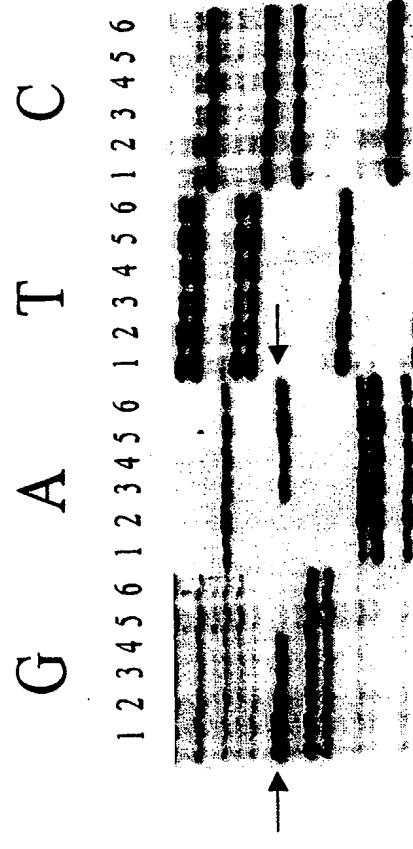


Fig. 2c

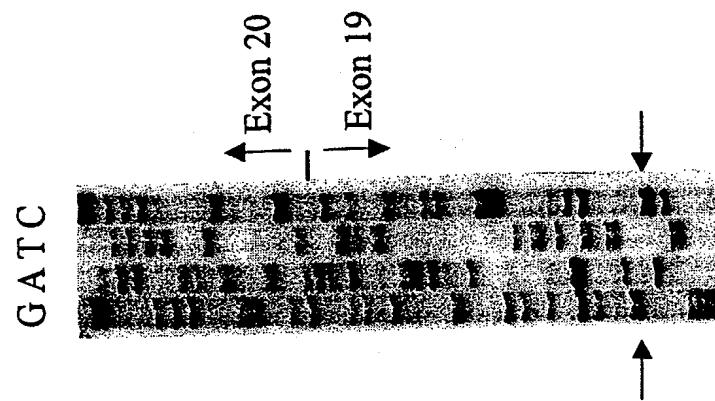


Fig. 2b

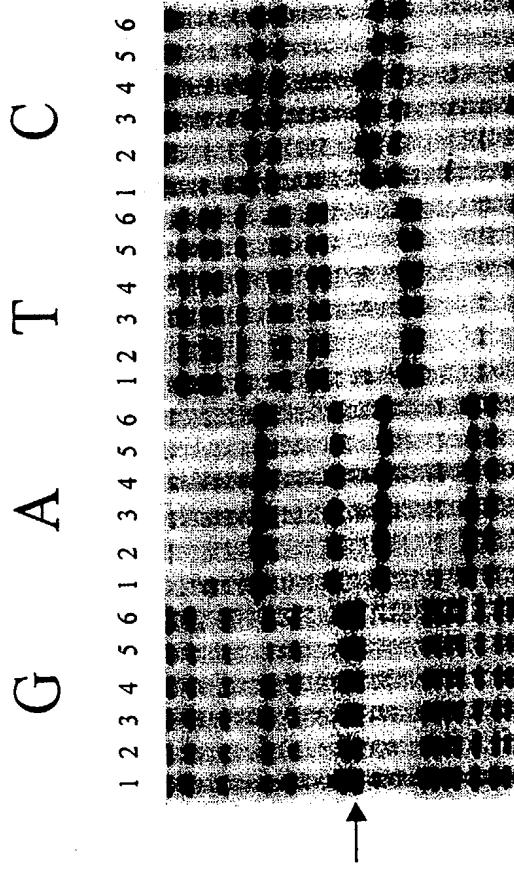


Fig. 3A

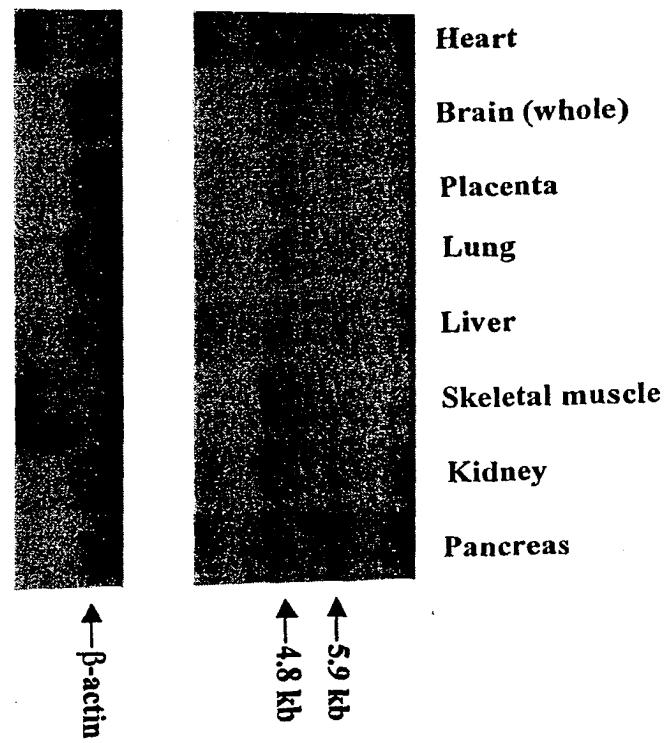


Fig. 3B

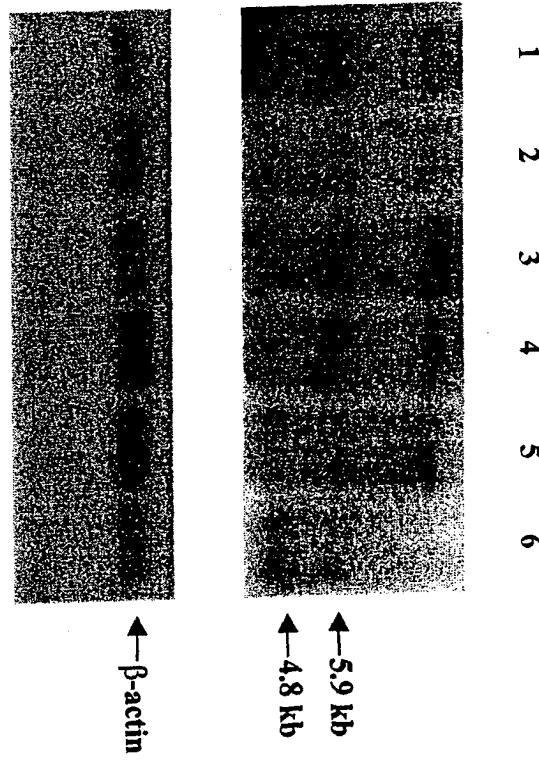


FIG. 4A

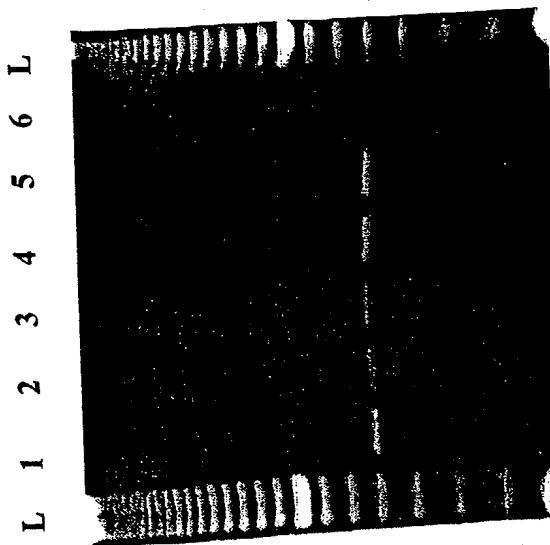
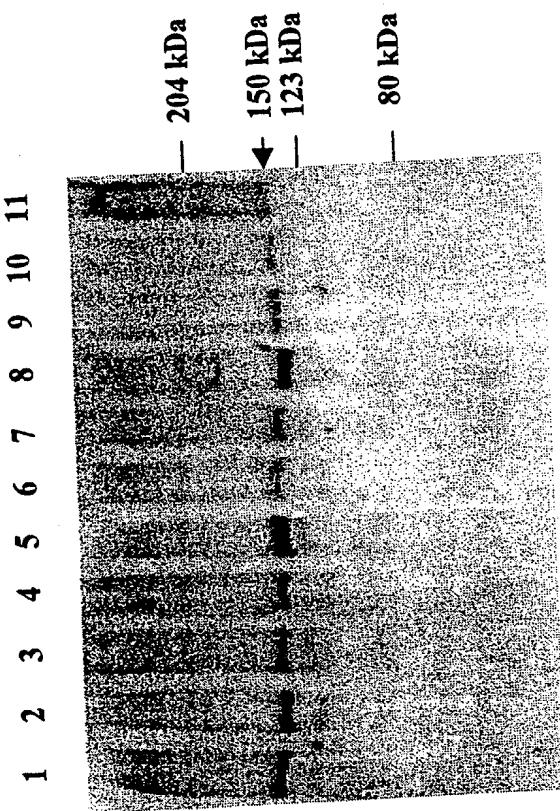


FIG. 4B



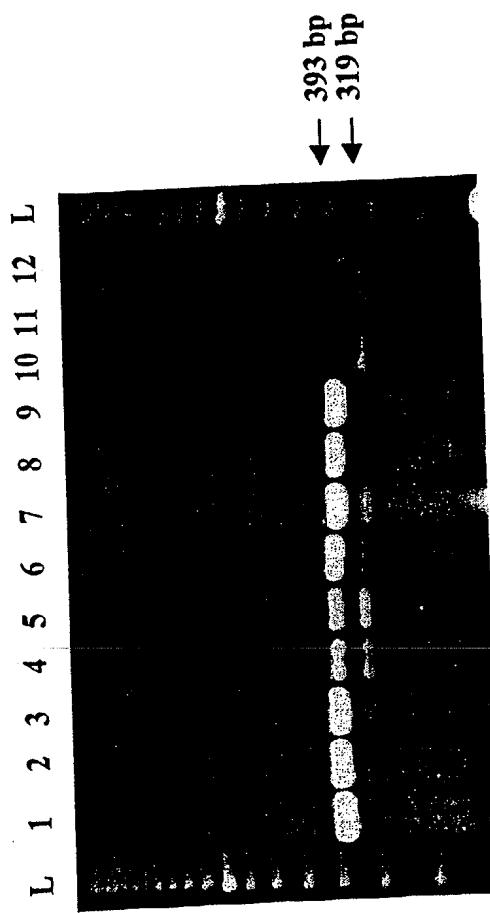


FIG. 5

FIGURE 6

IKBKAgenomic.seq Length: 66479

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55601 CCCCTAACTG AACTGGGAGA GATGCTTAAG CCAGGATAAA GAATTGTGGG
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FIGURE 7

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Figure 7
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3181 cttcccagaa tgcttaaact tgataaaaaga taaaaacttg tataacgaag ctctgaagtt
3241 atattcacca agctcacaac agtaccagga tatcagcatt gcttatgggg agcacctgat
3301 gcaggagcac atgtatgagc cagcgggct catgtttgcc cgttgcgggt cccacgagaa
3361 agctctctca gccttctca catgtggcaa ctggaagcaa gccctctgtg tggcagccca
3421 gcttaacttt accaaagacc agctggtggg cctccggcaga actctggcag gaaagctgg
3481 tgagcagagg aagcacattg atgcggccat ggtttggaa gagagtgcgg aggattatga
3541 agaagctgtg ctcttgctgt tagaaggagc tgcctggaa gaagcttga ggctggata
3601 caaatataac agactggata ttatagaaac caacgtaaag ccttccattt tagaagccca
3661 gaaaaattat atggcatttc tggactctca gacagccaca ttcagtcgcc acaagaaaacg
3721 tttattggta gttcgagagc tcaaggagca agcccgacag gcaggtctgg atgatgaggt
3781 accccacggg caagagtca gaccttctc tgaaaactagc agtgcgtga gtggcagtga
3841 gatgagtggc aaatactccc atagtaactc caggatatca gcgagatcat ccaagaatcg
3901 ccgaaaagcg gagcggaaaga agcacagcct caaagaaggc agtccgctgg aggacctggc
3961 cctcctggag gcactgagtg aagtggtgcgaa acactgaa aacctgaaag atgaagtata
4021 ccatattttt aaggtaactt ttctctttga gtttgcataa caaggaaggg aattacagaa
4081 ggcctttgaa gatacgtgc agttgatgaa aaggtcaattt ccagaaattt ggactcttac
4141 ttaccagca aattcagcta ccccggttct aggtcccaat tctactgcaaa atagtatcat
4201 ggcacatctt cagcaacaga agacttcggg tccctgttctt gatgctgagc ttttataacc
4261 accaaagatc aacagaagaa cccagtggaa gctgagcctg ctagactgag tgactgcagt
4321 taggagggat ccgacagaga agaccatttc cactcattcc tggatcataa ccaccccttgc
4381 ctcttgagg gctggctatt gagaactgga aagagtaaaa tgataactta ccttagcatt
4441 gccaagaact tcagcagaca acaagcaattt ctatttattt tatgttgcgtg atacatcttgc
4501 atcatttagca agacattaag cttaaccat tatggcacca ttttgcataa atgattgttc
4561 ttcaacttg gctgttttag agcataattt tggtaatcat gagattaatg ttcatgatt
4621 tctacacttca aagtgtgaag acaagtaaaa caatgtttctt aaattgttctt attttgcgtt
4681 cgagaagat tacaatggct attagtgcata cattttgtca aatgtatcata cttaaatagc
4741 ttcttgacat cttaaactaa agcagaataa aaagtatcctt ttgaaattat aagcccttgc
4801 ttgctgacag ctatttattt gtaacatctt accaggtcat gtcgtttcag ttataactgg
4861 gctgagccctc ctataattac aatgtctata gggactgttt tactgcctgt gtatttctg
4921 ctagagagt agcaatgtt aagctgaaac agattagaat ttctaaacag tatcatgcac
4981 agttgggtgt agtgatcagt gtgcattgtt tggcatgcat gtttgcataa tattctctgt
5041 tctccaaata ctgtttctt aactcagata tttttgttag tggatcataa acttcattta
5101 tttttcgta tggacttta ctgacttctc tttattcaat tctccacgccc ctcaccaaaa
5161 aaaaactgtct caaaatgaga atattttat tcttcattgtt gagtctagaa aacgccccac
5221 ttcattctga ttaaaaaattt cttccatgtt tttaatatac agaaccagac ctttcttact
5281 gtgtatctta gcccattgt gtctctataa caacaaccag ctttcaaaagg aactaataga
5341 gtgaaaactc actcattacc acgaggatgg cacaagcgat tcacgttaga tctgcccctg
5401 tgaccaaaac acctccctt gggcccccact tccaaacactg gtatcataat ttcaacatga
5461 gttttagggaa aacaaatgcc taaactacag cactgtacat aaactaacag gaaatgtgc
5521 ttttgcataat cttttttttt aattttttttaa aattttttttttaa aattttttttttaa
5581 agcaagatgt taactataga atcaatctag gaggattcac tggatcataa aactttctg
5641 tatgtttgaa cattttcaca atctcatagg agttttttttttaa aagaagagaa agaagatata
5701 ctttgctttt gggatcataa cttttttttttaa aattttttttttaa aattttttttttaa
5761 tattgaaagg ctgcaagtac tttgtatca ctctttggca tggatcataa aacatggtaa
5821 ctttatattttaa aatatagtgc tcttgctttt gataactgtt aaggggatcataa tgctgtat
5881 ctggaaatag aagtaaatgtt gtttattgaa aaaaaaaaaaaa aaaa

FIGURE 8

1 mrnlklfrtl efrdiqgpgn pqcfslrteq gtvligsehg lievdpsre vknevslvae
61 gflpedgsgr ivgvqdlldq esvcvatasg dvilcslstq qlecvgsvas gisvmswspd
121 qelvllatgq qtlimmtkdf epileqqihq ddfgeskfit vgwgrketqf hgsegrqaaf
181 qmcmhesalp wddhrpqvtw rgdgqffavs vvcpetgark vrvwnrefal qstsepvagl
241 gpalawkpsg sliastqdkp nqqdivffek nglhghftl pflkdevkvn dllwnadssv
301 lavrledlgr ekssipktcv qlwtvgnhyhw ylkqslsfst cgkskivslm wdpvtpyrlh
361 vlcqgwhyla ydwhwtdrs vgdnssdl.sn vavidgnrwl vtvfrqtvvp ppmctyqlif
421 phpvnqvtfl ahpqksndla vldasnqisv ykcgdcpsad ptvklgavgg sgfkvclrt
481 hlekrykiqf ennedqdvnpl lkiglltwie edvflavshs efsprsvihh ltaassemde
541 ehgqlnvsss aavdgviisl ccnsktsvv lqladggifk ylwespslai kpkwnsggfp
601 vrfpypctqt elamigeeec vlgltcrclf findieasn itsfavydef llltthshc
661 qcfcldrasf ktlqaglssn hvshgevlrk vergsrivtv vpqdtklvlq mprgnlevvh
721 hralvlaqir kwldklmfke afecmrklri nlnpiydhnp kvflgnvetf ikqidsvnhi
781 nlfftelkee dvtktmypad vtssvylsrd pdgnkidlvc damravmesi nphkyclsil
841 tshvkkttpe leivlqkvhe lqgnapsdpd avsaaealky llhldvnel ydhslgtydf
901 dlvlmvae ks qkdpkeylpf lntlkkmetn yqrftidkyl kryekaighl skcgpeyfpe
961 clnlikdknl ynealklysp ssqqyqdisi aygehlmqeh myepaglmfa rcgahekals
1021 afltgcnwkg alcvaqlnf tkdqlvglr tlagklveqr khidaamvle esaqdyeeav
1081 llllegaawe ealrlvykyn rldietnvk psileaqkny mafldsqtat fsrhkkrllv
1141 vrelkeqaqq aglddevphg qesdlfsets svvsgsemsg kyshsnsris arssknrrka
1201 erkkhsikieg spledlalle alsevvqnte nlkdevyhil kvlfefefde qgrelqkafe
1261 dtlqlmersl peiwtltyqq nsatpvlgn stansimasy qqqktsvpvl daelfippki
1321 nrrtqwkls1 ld

M_musculus	1	-----	MRNLKLFRTLEFRDIQAPKPF	QCFCLRAT	QGTVLIG
H_sapiens	1	-----	MRNLKLFRTLEFRDIQGPNP	QCFSLRAT	QGTVLIG
D_melanogaster	1	-----	MRNLKLFRTYC	QHLLQPELNGG	SDIY
S_cerevisiae	1	MVEHDKSGSKRQELRSN	MRNLITLNKGKEKPTAETAEGLDEDDISFTLDE	WFTLDSIT	
A_thaliana	1	-----	MKNLKLFSERP.QMOLHSTEAVQFAAEDDQSLFFFSSAN		
C_elegans	1	-----	MKNLKLFSERP.QMOLHSTEAVQFAAEDDQSLFFFSSAN		
M_musculus	37	SERLGLTEVDP..VRREVKT	SLVAEGFLPEDGSGCIVG	QDQESVCVATASGDV	IV
H_sapiens	37	SEHGLIEVDP..VSREVKNE	SLVAEGFLPEDGSGRIVGV	DQESVCVATASGDV	IV
D_melanogaster	36	FVYDNKTYA..VQESGDV	RKLFADL..LPE..	IVGVFELQLDN	IV
S_cerevisiae	61	CVLGSTDHIGA	QESRMDTDDKQVSVRFADINO	QVFVFEQGD	IV
A_thaliana	43	FVYALQSSFQNE	SAGAKSAMPEEVCSIDIEP	FITFDFDAAKESHL	IV
C_elegans	27	PELQQTIAVSK	NELLITENNLISSTIKWAEQRRELE	TSRPTDQGQEV	IV
M_musculus	95	C.....NLSTQQLECVGSVASGIVMSWSPDQEL	LLLATRQQT	QIMMTKDFE	VIAEGQ
H_sapiens	95	C.....SLSTQQLECVGSVASGIVMSWSPDQEL	LLLATRQQT	QIMMTKDFE	VIAEGQ
D_melanogaster	87	V.....SQTGATSEGTCDFGVI	EMI	FTVTRTHAAMT	STFVIAEOP
S_cerevisiae	121	ATYDPVSLP	RTETEINGIDNGI	AAQSVDETL	IVTKDRN
A_thaliana	102	..HNVERSDVTEFVG	NIGGKCIISPNTG	LLGQD	IVMTYDWALY
C_elegans	87	VEDGEVMD.....LEIAELTD	ATVSAAEWTADE	STLALADN	IVTLYADSSLV
M_musculus	148	T.HQDDFGEGKF	VTVGWSKQ	TOFHGSEGRP	IAFPV
H_sapiens	148	T.HQDDFGESKF	VTVGWSKQ	TOFHGSEGRP	QAFQ
D_melanogaster	140	T.DAFLDPEQOF	VNVVGWKK	KETOFHGSEGRQAAK	K
S_cerevisiae	181	L.EVDDLKISKH	VTVGWKK	KETOFNGKAR	AMEREAAASLKA
A_thaliana	155	L...GEVPEGGVVRET	ASLQ	IVYKA
C_elegans	140	LIFSEWERKSAPVN	VVGWSESTQFNGSAG	KLKPGEKIEKEK	.
M_musculus	195	R.....PH..	IHWWRGDG	EYFAVSVVCROTEARKIRV
H_sapiens	195	R.....PH..	IHWWRGDG	EYFAVSVVCPTGARKIRV
D_melanogaster	187	L.....NQEN	ENISWWRGDG	EYFAVSVVAAQLS
S_cerevisiae	240	TGEVT	TDSSHEIP	ENISWWRGDCEYFAVSVAAQLS
A_thaliana	168NDI	SYNCGGISISWWRGDG	KYFATRTFVYDSE
C_elegans	181EQE	QHSKTKTS	YHWRWDGEIVAVSFGKLNHTY
M_musculus	235	E	SVPGGLGPALAWKPSGS	SLIASTQDKPNOODWVFFEKNG
H_sapiens	235	E	EVAGLGPALAWKPSGS	SLIASTQDKPNQODIVFFEKNG
D_melanogaster	229	EKSANLKD	SMVWRPQ	GNWIAVPOQFPNKSTIALFEKNG
S_cerevisiae	299	E	EVPGVNEHOL	WPKPQGS	SLIASTQDK
A_thaliana	219	E	ETKEFTQGILE	WMPSG	TDLGEESV
C_elegans	230	E	IRNIYLSHCF	AKPKNSDDSSPSIAFF
M_musculus	289	...	VNDLLWN	ADSSVLAIWEGLHGHFTLPFLK
H_sapiens	289	...	VNDLLWN	ADSSVLAIWKDEVK
D_melanogaster	283	...	VVQLRWS	EDSDMLQDZP
S_cerevisiae	357	...	VE	SMCWNLQDZP
A_thaliana	277	...	CENIKLWN	NSASDLIA
C_elegans	286	...	RRIEKE	WENSTGTLQDZP
M_musculus	346	I	VSILHWDP..VTPCRLH	VLCWVFTVGN
H_sapiens	346	I	VSILMWDP..VTPMRLH	VLCWVFTVGN
D_melanogaster	331	I	VALLHWDP	TRCGWVFTVGN
S_cerevisiae	398	I	SYK	KWHPWVFTVGN
A_thaliana	325	I	VVIMWDP..	TKPLOLICWTLSWVFTVGN
C_elegans	334	I	SHWKW	STVECQNTWVFTVGN
M_musculus	404	F	Q	TPVPPPMCTY	YRLLIPHPVNQIVF
H_sapiens	404	F	Q	TPVPPPMCTY	YRLLIPHPVNQIVF
D_melanogaster	384	F	Q	TPVPPPM	SKE..LQKPL
S_cerevisiae	455	L	AL	IVVPPPM	YYRDFETEGNVL
A_thaliana	376	L	LSL	LSL	YRDFETEGNVL
C_elegans	387	L	LCRRV	VPPPMCDY	YRDFETEGNVL
M_musculus	457	M	D	STVKL	GAVGGNGFKVPL
H_sapiens	459	A	D	PTVKL	GAVGGNGFKVPL
D_melanogaster	420	A	D	SPHYLLA	THSSAG
S_cerevisiae	514	I	D	PKSEFT	SEESLROQAF
A_thaliana	427	I	D	PTWEDLEGKDF	SVEISDCKT
C_elegans	445	I	D	FRKKYILEIKVPSH	KTYFRCFA
				SQTDTGKYF
				NSDRASIDEV
				LHTEVTEG
				ICG

FIG. 1. Comparison of the amino acid sequence of Ikap across several species. Alignment of the amino acid sequence of Ikap (M_musculus) with that of *Homo sapiens* (H_sapiens), *Drosophila melanogaster* (D_melanogaster), *Saccharomyces cerevisiae* (S_cerevisiae), *Arabidopsis thaliana* (A_thaliana), and *Caenorhabditis elegans* (C_elegans). Black boxes indicate identical AA, while conserved AA residues are shown in gray. Asterisk (*) at AA position 696 for mouse and human proteins indicates the location of the heterozygous R696P mutation found in only 4 FD patients. Sequence alignments were made using Pileup and Boxshade commands from GCG Wisconsin Package V.9.0 (Madison, WI).

Figure 9

Figure 9
Continued

<i>M_musculus</i>	1062	HSEAAATVLEGYAQDYEEAVLLLLEGSAWEELRLVYKYDRVDIIE	TSHKPSILEAQKNYM
<i>H_sapiens</i>	1062	HETAAAMVLEESAQDYEEAVLLLLEGSAWEELRLVYKYNRD	IIETTNVKPSILEAQKNYM
<i>D_melanogaster</i>	949	HMEAVEETKHCQDRKRQFDVLE	GHLYSRAYEAGLED. DD
<i>S_cerevisiae</i>	1096	YIENDTQLEYLDNVKEAVLYCK	TYRYIIASLVAIKAKED. EEVVDPG. GEGFGIMA
<i>A_thaliana</i>	1061	PAEAAKTALEYCSDISGQESLLN	REWEELRVA
<i>C_elegans</i>	1008	PKEBLAKALKLASSSTIVHMLC	FEWLPSREVEVGK. . . . BEAKKIALSRNDE
<i>M_musculus</i>	1122	DFLDSETATFIRHKNRLOVVRALR	RAPOVHYDHEVHGPESDLE. SETSSIS. GSEMS
<i>H_sapiens</i>	1122	DFLDSETATFSRHKKRLLVVR	ELKEOAQAGIDDEVPHGQESDLE. SETSSIS. GSEMS
<i>D_melanogaster</i>	1007	SSLQNLQLFEDYKORLID	RRNQAKSGEEDTIV. NLKEVDIL. SETSSHS. SPPYS
<i>S_cerevisiae</i>	1156	ELIADCKEQQINSQLRRLRE	GRAKKEENPYAFYGETQADDEVSAPSETSEQESFFRY
<i>A_thaliana</i>	1120	SEFKESIEKVGKVLT	RLAVRCRELLAALKSERSVVVDLDDDTASEASSNQSGMSAYI
<i>C_elegans</i>	1063	MDEERRKTEFENYKKRLAVVRENKLKRVE	QFAAGEV. . . . DDLRDEISVISSISR. . .
<i>M_musculus</i>	1180	.GKYSHSNR. ISARSSKNRR. . .	KAERKKHSLKEGSPLEGLALLEAL. . . . SEVVO. SVE
<i>H_sapiens</i>	1180	.GKYSHSNR. ISARSSKNRR. . .	KAERKKHSLKEGSPLEGLALLEAL. . . . SEVVO. STE
<i>D_melanogaster</i>	1063	.GTSRKTKG. . .	FRSSSKNRR. . . KHERKLFSLKPGNPIEDHALNEVAKHAO. DQD
<i>S_cerevisiae</i>	1216	.GKTGGGAKKGA	SRRRKKNKR. . . EERKXARGKKGTYEE. . . BYLVQSVG
<i>A_thaliana</i>	1180	LCTRRCGSIASVSSN	ISARLDLRRRKSGKERRAGSAGEMALMCHL. . . . KGR. MTC
<i>C_elegans</i>	1115	SGSSKISMASTVRRRK. QIEKKKSSLKEGGEYEDSALLNVLSE	NYRWEENIGSE
<i>M_musculus</i>	1231	KLKDEVRAILKVLFLFEEQ	QAKELQRAFESTLQLMERAVPEIWTPEAQQSS. ATPVLG
<i>H_sapiens</i>	1231	NLKDEVYHILKVLFLFEEQ	ELQRAFESTLQLMERAVPEIWTPEAQOONS. ATPVLG
<i>D_melanogaster</i>	1116	PYSDTCKA	QLOANAADADPLAALQREFKTLLOAMQAADEBIWTB
<i>S_cerevisiae</i>	1268	QTKPDAVRMEGE	CRRNMRQAAQKQKNEVEVLDDLEKANVREIVSIS
<i>A_thaliana</i>	1234	GGKREI	KSILICLVTLGEMESAQKLOQIAEN. FOVSQVMAVDE. HDTVSS
<i>C_elegans</i>	1168	FCFPWNFNL	SESVDEEVYC
<i>M_musculus</i>	1289	PSSSTANSI	IASYQQQKTCVPLDAGVMPPKMPPRQWKLSSL
<i>H_sapiens</i>	1289	PNSTANSI	IASYQQQKTSVPMLDAEFFIPPKINRPRQWKLSSL
<i>D_melanogaster</i>	1176	PN. VDYE	YLOKEORYPLISPLKR. . . FKPQLI. . . MMDWQHEELC
<i>S_cerevisiae</i>	1326	EVYYIPE	PVPEIHDFPKSHYDF
<i>A_thaliana</i>	1292	FERY	QKTRSEARDSDFTSWMLK. . . VFISP-----
<i>C_elegans</i>	1178	-----	-----

Figure 9
Continued

TABLE 2. COMPARISON OF THE NOVEL MOUSE *Ikkkap* GENE WITH MULTIPLE SPECIES HOMOLOGS

Species	Gene name	No. of amino acids	Molecular weight (kDa)	% aa identity with M.m.	GenBank Accession No.
<i>Mus musculus</i> (M.m.)	<i>Ikkkap</i>	1332	149.11	—	AF367244
<i>Homo sapiens</i>	<i>IKBKAP</i>	1332	149.11	80	AF153419
<i>Drosophila melanogaster</i>	<i>CG10535</i>	1213	138.21	32	AAF54670
<i>Saccharomyces cerevisiae</i>	<i>Elp1/Iki3p</i>	1349	152.99	29	AAB67278
<i>Arabidopsis thaliana</i>	Unknown	1308	146.63	27	BAB08695
<i>Caenorhabditis elegans</i>	Unknown	1177	134.80	24	AAF60430

Figure 10

TABLE I. MOUSE *Ikbkap* EXON AND INTRON BOUNDARIES

Exon	Acceptor site	Donor site	Size (bp)	cDNA position
1		AGgtgagcatteggccg	129	1..129 ^a
2	tttttttccctcagAA	AAgttaggtcaactgtatgc	163	130..292 ^b
3	tatgttttgtgaaagGT	AGgttaggtgtaaaggct	153	293..445
4	ttttctctgtatgcagCT	AGgttaaccttgcactg*	82	446..527
5	acatgaacctaaagCT	AGgttaaggcttctgtgg	81	528..608
6	cttggaaaaactgttagGC	TGgttagggccggat	86	609..694
7	ggtgtctcttcagCC	TGgtgtctcttcag*	97	695..791
8	ctacccttcgtcagAG	AAgtgagtgacataaa*	91	792..882
9	agggttcgtttcagAC	AGgttaggggtcagat	124	883..1006
10	ttttgtcccttacccagGT	TGgtatgtacacgttgc	94	1007..1100
11	tccctccacacacagTC	AAgttaagggtgtcgaa	231	1101..1331
12	tttttcattgttagAC	TGgttaagtggaaagcagg	165	1332..1496
13	tttttttttttcgttagGT	TCgttaagtccctaaata	100	1497..1596
14	ctaataatttgcacacAG	AGgtatcatgttgcac	189	1597..1785
15	tttttttttttttttagTT	GGgttagggatcagat	107	1786..1892
16	tttaatcttacaacacAG	AGgttaatagacacggc	104	1893..1996
17	ttcattttttcgtcagGA	AGgtatgtaggcttgcgt	54	1997..2050
18	tcttgcctgtgcagGT	AAgttaaccttccctata	106	2051..2156
19	cactgggttttttagTG	AGgttaactgtacttc*	116	2157..2272
20	gggtttttttttagAT	AAgttaagtatttttct*	74	2273..2346
21	ttcctgttcttacacAG	AGgtacactttgcgtct	79	2347..2425
22	tacttttttttagatGT	AGgttaagtattttgtata*	80	2426..2505
23	tactgttttttttttagGG	AAgtgggtgtgtgtt	138	2506..2643
24	cacttacttacccatAGT	AGgttagagatccgcgc*	86	2644..2729
25	cttaaaatccaaacagGA	AGgtatgtggatgttag*	149	2730..2878
26	aacttttttcgttagGA	TGgttaagggttttttt	124	2879..3002
27	tttttttttttttcgtGA	AGgtatgtgtgggtta*	98	3003..3100
28	cgctctttgttacacAGC	AGgttaaggccggccatt	202	3101..3302
29	tttgttttttttcgtGA	AGgttagctcccccgg	62	3303..3364
30	ctttttccctgtcagGA	TGgttagggaaagcttga	63	3365..3427
31	ttttttccctttttagGT	AGgtgaggatcattt*	61	3428..3488
32	attatgcatcttcgtcagCC	GGgttaggtgtccaaaa*	114	3489..3602
33	gttcatcttttttttagAT	GCgtactgttgcggact*	112	3603..3714
34	tgttaattttgtacacAG	AGgtatgttttttttttt	128	3715..3842
35	ccattttttttttttagAT	CGgttagtttttttttttt	155	3843..3997
36	ctgttttttttttttagGT	CGgtgtactgttttttt	76	3998..4073
37	catttttttttttttagAT	TTtttttttttttttttttt	709	4074..4799 ^c

Figure 11

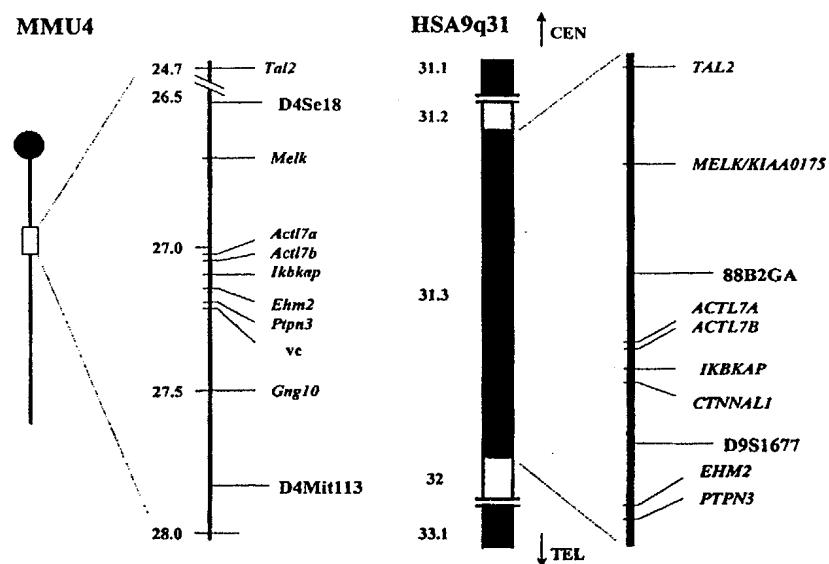


Figure 12